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<!--StartFragment-->RESULT 44
AAU78439
ID    AAU78439 standard; peptide; 35 AA.
XX
AC    AAU78439;
XX
DT    18-JUN-2002 (first entry)
XX
DE    Inhibitor of apoptosis (IAP) protein Smac, peptide Smac-N35.
XX
KW    Human; inhibitor of apoptosis; IAP; Smac; apoptosis; BID; BIR1; BIR2;
KW    Bcl2 interacting domain; caspase; BIR domain; BIR3; gene therapy;
KW    neoplastic cell; tumour.
XX
OS    Homo sapiens.
XX
PN    WO200216418-A2.
XX
PD    28-FEB-2002.
XX
PF    24-AUG-2001; 2001WO-US026492.
XX
PR    24-AUG-2000; 2000US-0227735P.
XX
PA    (UYJE-) UNIV JEFFERSON THOMAS.
XX
PI    Alnemri ES;
XX
DR    WPI; 2002-304115/34.
XX
PT    Novel Smac peptides and polynucleotides encoding the peptides, useful for
PT    stimulating apoptosis in neoplastic or tumor cell which overexpresses
PT    inhibitor of caspase, and for identifying apoptosis modulating compounds.
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PS    Example 4; Page 47; 78pp; English.
XX
CC    The invention relates to an isolated Smac peptide or polypeptide (I) and
CC    an isolated nucleic acid (II) encoding (I). Also described is a method of
CC    identifying a compound that inhibits apoptosis, comprising: (a)
CC    separately contacting several cell populations expressing a cytosolic
CC    Smac (a Smac isoform that begins with MKSDFYF sequence, replacing the
CC    mitochondrial targeting sequence (residues 1-55 of (I)), and residues 56-
CC    60 of (I)) and an inhibitor of BID (Bcl2 interacting domain) with a
CC    compound to be tested for apoptotic inhibiting activity; (b) incubating
CC    the cell populations with a direct stimulus of the cell death pathway;
CC    and (c) measuring the specific apoptotic activity of the cell
CC    populations, where inhibition of the specific apoptotic activity is
CC    indicative that the compound is an inhibitor of apoptosis. (I) and (II)
CC    are useful for inducing apoptosis in a cell. The Smac polypeptide and
CC    polynucleotide are useful for stimulating apoptosis in a neoplastic or
CC    tumour cell which overexpresses an inhibitor of caspase, where the
CC    inhibitor inhibits activation or activity of caspase-3, caspase-7 or
CC    caspase-9. Preferably, the cell overexpresses at least a portion of IAP.
CC    (I) is useful for identifying an inhibitor or enhancer of a caspase-
CC    mediated apoptosis which involves contacting a cell transformed or
CC    transfected with a vector expressing (I) with a candidate inhibitor or
CC    candidate enhancer; and detecting cell viability, where an increase in
CC    cell viability indicates the presence of an inhibitor and a decrease in
CC    cell viability indicates the presence of an enhancer. Optionally, the
CC    method involves detecting the presence of large and small caspase
CC    subunits after contacting cell transformed with the vector expressing

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CC (I), with the candidate compound. A decrease in processing indicates the
CC presence of an inhibitor and an increase in the processing indicates the
CC presence of an enhancer. Preferably, the large and small subunits of
CC caspase-3, caspase-7 or caspase-9 are detected. (I) is also useful for
CC identifying a compound that inhibits Smac binding to Smac-binding
CC molecule (a portion of IAP e.g. a BIR domain such as BIR1, BIR2 or BIR3,
CC or a full-length IAP). (II) is useful in gene therapy techniques. The
CC present sequence represents the amino acid sequence of Smac peptide Smac-
CC N35

XX

SQ Sequence 35 AA;

Query Match 100.0%; Score 33; DB 5; Length 35;

Best Local Similarity 100.0%; Pred. No. 3.3;

Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 AVPIAQK 7

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Db 1 AVPIAQK 7

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